Serial No.: 09/532,708
Filed: March 22, 2000

REMARKS

Claims 12, 16-18, 20, 22, 28, and 33 have been amended. Claims 12-24, 28, 33, and 49 are pending in the application.

The Commissioner is authorized to charge any additional fees including extension fees or other relief which may be required, or credit any overpayment to Deposit Account No. 06-1300 (Our Order No. A-64580-4/RFT/NBC).

Please direct any questions to the undersigned at (415) 781-1989.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

12. (Amended) A method of high throughput integrated genomics comprising:
    a) providing a plurality of enhanced homologous recombination (EHR) compositions, wherein each composition comprises:
        i) a recombinase;
        ii) a first and a second targeting polynucleotide, wherein said first targeting polynucleotide comprises a portion substantially complementary to a fragment of a target nucleic acid and is substantially complementary to said second targeting polynucleotide; and
        iii) a separation moiety;
    b) contacting said EHR compositions with [one or more] a library of target nucleic acids [sample(s)] under conditions wherein said targeting polynucleotides hybridize to one or more target nucleic acids [member(s)] of [one or more nucleic acid sample(s)] said library; and
    c) isolating and cloning said target nucleic acid(s) wherein said [providing] isolating and [contacting] cloning are [done] performed using a robotic system.

16. (Amended) The method according to claim [1]12, wherein said target nucleic acid comprises single-polynucleotide polymorphisms.

17. (Amended) The method [of] according to claim [1]12 , wherein said library of target nucleic acids comprises all or part of a cDNA library, genomic DNA library, genomic DNA samples, or combinations thereof.

18. (Amended) The method of claim 17, wherein said genomic DNA samples are [library is] from [a single] one or more organisms.

20. (Amended) The method according to claim 19 wherein at least one of said making, introducing and performing steps [are]is [done] performed using a robotic system.

22. (Amended) The method according to claim 21 wherein at least one of said making, adding, and determining steps [are]is [done] performed using a robotic system.

28. (Amended) The method according to claim [26 or 27] 12 further comprising[:] sequencing said [expressed] target nucleic acid.

33. (Amended) The method of claim [1, 13, 21, 23, 25, 26, 27, 28, 31 or 32]12, wherein

said robotic system comprises a computer workstation comprising a microprocessor programmed to manipulate a device selected from the group consisting of a thermocycler, a multichannel pipettor, a sample handler, a plate handler, a gel loading system, a gene sequencer, an automated transformation system, a colony picker, a bead picker, a cell sorter, an incubator, a light microscope, a fluorescence microscope, a spectrofluorimeter, a spectrophotometer, a luminometer, a CCD camera and combinations thereof.

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Pending Claims 12-24, 28, 33, and 49 as Amended

C1

12. (Amended) A method of high throughput integrated genomics comprising:
    a) providing a plurality of enhanced homologous recombination (EHR) compositions, wherein each composition comprises:
        i) a recombinase;
        ii) a first and a second targeting polynucleotide, wherein said first targeting polynucleotide comprises a portion substantially complementary to a fragment of a target nucleic acid and is substantially complementary to said second targeting polynucleotide; and
        iii) a separation moiety;
    b) contacting said EHR compositions with a library of target nucleics acid under conditions wherein said targeting polynucleotides hybridize to one or more target nucleic acids of said library; and
    c) isolating and cloning said target nucleic acid(s) wherein said isolating and cloning are performed using a robotic system.

13. The method according to claim 12, wherein said target nucleic acid is a target gene.

14. The method according to claim 13, wherein said target nucleic acid is a portion of said target gene.

15. The method according to claim 12, wherein said target nucleic acid is a regulatory sequence.

C2

16. (Amended) The method according to claim 12, wherein said target nucleic acid comprises single-polynucleotide polymorphisms.

17. (Amended) The method according to claim 12, wherein said library of target nucleic acids comprises all or part of a cDNA library, genomic DNA library, genomic DNA samples, or combinations thereof.

18. (Amended) The method of claim 17, wherein said genomic DNA samples are from one or more organisms.

19. The method according to claim 12 further comprising:
    d) making a library of nucleic acid variants of said target nucleic acid;
    e) introducing said library of nucleic acid variants into a cellular library; and
    f) performing phenotypic screening on said cellular library.

C3

20. (Amended) The method according to claim 19 wherein at least one of said making,

C3 cont'd

introducing and performing steps is performed using a robotic system.

21. The method according to claim 12 further comprising:
d) making a plurality of cells comprising a mutant target nucleic acid;
e) adding a library of candidate agents to said plurality; and
f) determining the effect of said candidate agents on said cells.

C4

22. (Amended) The method according to claim 21 wherein at least one of said making, adding, and determining steps is performed using a robotic system.

23. The method according to claim 21, wherein said mutant target nucleic acid is a gene sequence knock-out or a gene sequence knock-in.

24. The method according to claim 21, wherein said mutant target nucleic acid comprises an insertion, substitution, deletion or combinations thereof.

C5

28. (Amended) The method according to claim 12 further comprising sequencing said target nucleic acid.

C6

33. (Amended) The method of claim 12, wherein said robotic system comprises a computer workstation comprising a microprocessor programmed to manipulate a device selected from the group consisting of a thermocycler, a multichannel pipettor, a sample handler, a plate handler, a gel loading system, a gene sequencer, an automated transformation system, a colony picker, a bead picker, a cell sorter, an incubator, a light microscope, a fluorescence microscope, a spectrofluorimeter, a spectrophotometer, a luminometer, a CCD camera and combinations thereof.

49. The method of claim 17, wherein said genomic library comprises a combination of multiple organisms.